Reemerging Pathogens

JUNE E. OSBORN, MD, *Ann Arbor, Michigan*

Respect for infectious diseases has been rekindled in the past few years, ignited by a growing recognition of microbial emergence and adaptability. The appearance of newly recognized pathogens with epidemic potential has been important in fostering a new sense of threat; and in particular, the human immunodeficiency virus (HIV) and the awful pandemic of the acquired immunodeficiency syndrome that it spawned have commanded attention, illustrating as they do the smoldering pathogenic potential of viruses that had heretofore been ecologically contained. The emergence of the Lassa, Marburg, Ebola, and Hantaviruses and the geographic expansion of the dengue virus have underscored the point that new infectious agents are out there and that the combined forces of urbanization, social destabilization, and global travel make it almost certain that more such novel challenges will appear.

Attention to these issues has been growing. The National Academy of Sciences produced a report in 1992 that lent credence and substance to those concerns; in 1995 the Institute of Medicine devoted the scientific session of its 25th annual meeting to the same theme. In addition, numerous symposia have been planned to address the general theme of emerging infections, including one that was sponsored by the University of California at San Francisco at the end of December 1995. Such enhanced awareness is heartening as a sign that the problem is now being taken seriously.

But focusing primarily on novel diseases and agents introduces a perceptive hazard, for the exotic element in the emergence issue tends to dominate. The Ebola virus causes lurid disease, and it comes and goes mysteriously—but somewhere else; in that instance, sustained importation is highly unlikely. Hantaviruses have appeared in the United States and in other parts of the world, but they have been geographically localized, quickly analyzed, and seemingly contained. The temptation is to remain detached from the issues thus raised or else to assume a nihilistic position, at least so far as the realities of medical practice are concerned, because sweeping global population changes and shifts in microbial ecology seem as far from individual practitioners' control as does the hole in the ozone layer.

Yet, the most profound threats stemming from microbial adaptability, in my view, are close to home: I refer to the relentless emergence of antibacterial and antiviral resistance capability among familiar, established human pathogens. The problem of bacterial resistance to previously reliably curative drugs has gone far beyond the simple strategy of switching antibiotics. Examples abound, including as an extreme case the fact that the haunting specter of enterococcal resistance even to vancomycin has become real, and the usefulness of generations of new antibacterial agents can be negated within months of their introduction. In fact, among the great bacterial infectious diseases, only syphilis remains fully susceptible to straightforward treatment protocols; for all the rest, reports are proliferating of microbial resistance against long lists of antibiotics.

There is little doubt that the pressure of antibiotic use throughout our environment has contributed to this unsettling trend, nor is there any question that antibacterial drugs are extensively overused both in the United States and worldwide. The public has developed an expectation that all febrile diseases require active therapy. The pressure on physicians to administer treatment is synergistic with the general momentum of defensive medicine. Furthermore, crowded appointment schedules make it tedious and unwieldy to undertake the necessary job of patient education about viruses and bacteria and the selective use of antibiotics.

That equation is shifting inexorably, however. We are now in a world where streptococci have turned aggressive, where pneumococci remain so, and where *Haemophilus influenzae* would be casting a truly ominous shadow on pediatric populations were it not for the remarkable efficacy (in terms of "herd immunity") of the new conjugated-polysaccharide vaccine. Of course, multidrug-resistant tuberculosis heads the list, if not in numbers, at least in the scale of alarm.

Mycobacterium tuberculosis serves as a useful focus to discuss what can be done. It is still the case that fully and continuously treated tuberculosis responds completely to established regimens. The problems have arisen when treatment has been discontinued or abbreviated and from growing pools of unduly susceptible hosts in whom mycobacteria can get an easy foothold—including those strains that have acquired the tricks of resistance to currently available antituberculous drugs. The good news is that old-fashioned strategies, such as directly observed

(Osborn JE: Reemerging pathogens, *In* Emerging and Reemerging Global Microbial Threats. West J Med 1996; 164:23-24)

From the University of Michigan School of Public Health, Ann Arbor.
Reprint requests to June E. Osborn, MD, University of Michigan School of Public Health, 109 S Observatory St, Ann Arbor, MI 48109-2029.

therapy to assure full and continuous treatment, have in fact stemmed the tide in places where they have been deployed. The scare about multidrug-resistant tuberculosis is by no means behind us, but there is reassurance in recent experience—and perhaps some old lessons to be relearned.

Until recently, the dominant response to problems of bacterial resistance—both for *M tuberculosis* and for the broader array of pathogens—has been a call for more antibacterial agents. Clearly, that will remain an important and necessary research goal for the foreseeable future, as the tide of resistant organisms swells, but as a sole response, it makes little sense. We should also devise and endorse with enthusiasm the changes in individual and group practices that would reduce the overuse of antibiotics and decrease their ubiquity in the environment (as, for instance, in agricultural feed as growth adjuncts). It surely is worth the time spent to educate patients about the specificity of antibiotic treatment and the unwisdom of keeping leftovers from prescriptions for self-medicating at a later date. The effect of such careless practices may be far from trivial.

Internationally, the over-the-counter availability of antibiotics makes the situation in this country pale by comparison. But there, too, concerted action may be possible and should be supported. At an Institute of Medicine meeting in October 1995, Stuart Levy, MD, Director of the Center for Adaptation Genetics and Drug Resistance at Tufts University School of Medicine (Boston, Massachusetts), told of the growing strength of an international collaborative group organized in 1981 and dedicated to fostering and sustaining a decrease in antibiotic use. Entitled the Alliance for the Prudent Use of Antibiotics, it now has participation from nearly 100 countries and has been increasingly effective in coordinating and sharing data about antibiotic use and resistance patterns around the world.*

It is heartening to know of that activity; such worldwide coordination of effort is surely going to be necessary because the fundamental dynamic of both emerging and reemerging infections is that of a world without biologic boundaries. The forces that have made it so—increasing population and migration, urbanization with its associated social upheaval, and international travel—will only intensify in the future.

A final note of concern: all that has been said about antibacterial agents pertains at least as much to antiviral drugs. The creation of clinically useful antiviral agents has proved difficult precisely because resistance arises so regularly—and sometimes quickly. At present, the number of licensed antiviral drugs is small, but they contribute importantly to the care of serious, chronic viral diseases: there are a few for HIV and fewer still for some of the human herpesviruses such as herpes simplex, varicella zoster, and cytomegalovirus. Yet, for each of them, the emergence of resistance has been recorded, and the transmissibility of resultant (resistant) viral strains has been documented.

As their usage expands, it will be important to draw the analogy to antibiotic lessons learned and to endorse and maintain clinical protocols that prevent—or at least forestall—the voiding of their usefulness. With such aspects of emerging and reemerging infections, effective response is not arcane or out of reach, and the practitioner community stands to play a critical role.

*For further information about this group, write to the Alliance for the Prudent Use of Antibiotics, PO Box 1372, Boston, MA 02117-1372.